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Normalization of Serum Lactic Dehydrogenase in β-Thalassemia Patients Following Bone Marrow Transplantation

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Serum lactic dehydrogenase (LDH) levels are mildly elevated in β-thalassemia major due to ineffective erythropoiesis. We reviewed the charts of 15 consecutive thalassemic children who underwent allogeneic, T-cell-depleted bone marrow transplantation (BMT) in our department during the last 3 years. Eleven patients had successful engraftment and are alive and well without evidence of disease, according to physical examinations, blood counts, and polymerase chain reaction (PCR) tests, with a median follow-up of 2 years. Two patients died due to transplantation-related complications, and two rejected the graft and received their backup autologous marrow. The LDH levels in the transplanted patients gradually decreased from an average of 952 ± 155 IU/L 10 days pre-transplant (N = 300–620) to 426 ± 56 IU/L at the day of transplantation, and stayed at approximately the same level post-transplant (489 ± 55 IU/L). By contrast, the LDH levels reverted to the pre-transplant value in those patients who rejected their marrow. The significance of this clinical observation for the pathophysiologic mechanism of intramedullary hemolysis and ineffective erythropoiesis in β-thalassemia major is discussed.

Key words: BMT, hemolysis, LDH, thalassemia

INTRODUCTION

Lactic dehydrogenase (LDH) is a known parameter for evaluating liver and lung tissue damage, as well as tumor mass, disease progression, and response to chemotherapy [1,2]. It is also known to be elevated in intravascular hemolysis [3,4]. LDH levels are quite high in β-thalassemia major as a consequence of ineffective erythropoiesis [4]. We recently noticed normalization of LDH levels in patients undergoing T-cell-depleted allogeneic bone marrow transplantation (BMT) for β-thalassemia and have therefore analyzed the charts of 15 consecutive patients, in order to establish and better characterize this phenomenon.

MATERIALS AND METHODS

Fifteen patients suffering from β-thalassemia major underwent T-cell-depleted allogeneic BMT in our department during the last 3 years. The median age was 7 years (range 2–11), 9 males and 6 females. Patients were conditioned with busulfan (16 mg/kg), thiothepa (5 mg/kg), cyclophosphamide (200 mg/kg), and total lymphoid irradiation (TLI) (200 cGY/day×5) or CAMPATH-1 IV (0.2 mg/kg/day × 4) and received a T-cell-depleted marrow (CAMPATH-1 rat antihuman, CDW52, monoclonal antibody kindly provided by Dr. G. Hale and Dr. H. Waldman, Cambridge UK,) followed by related HLA-matched BMT. Statistical analysis was performed using Student's *t*-test; *P*-values are given.

RESULTS

Eleven patients underwent successful transplantation. They are alive and well without evidence of disease,

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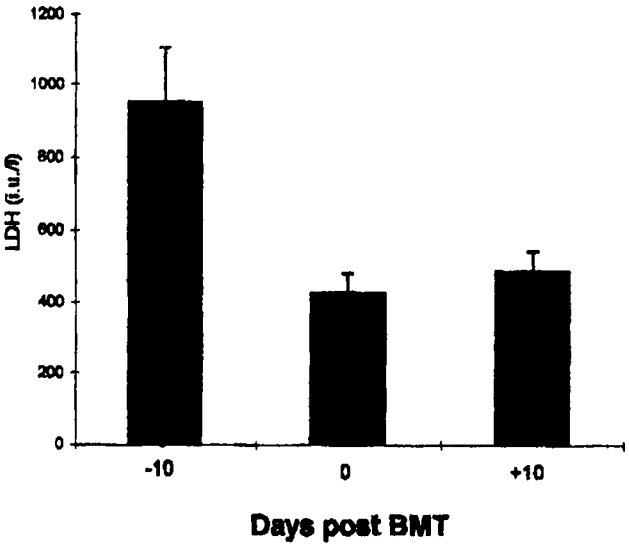

Fig. 1. LDH levels (IU/L) pre- (day −10), during (day 0), and post- (day +10) transplant in β-thalassemia patients (n = 11 ±SE). *$P < 0.001$.

according to physical examination, blood counts, and polymerase chain reaction (PCR) of the β-globin in the mutation area, with a mean follow-up rate of 2 years. In these patients, LDH levels decreased from an average of 952 ± 155 IU/L at day −10 pre-transplant, to 426 ± 56 IU/L at day 0, and remained at a level of 489 ± 55 IU/L at day +10 post-transplant and thereafter. Using the one-tailed, *t*-test for paired differences statistical test, LDH is significantly lower on day 0, in comparison to day −10 ($P < 0.001$). No statistical significance exists between the LDH levels on day +10 in comparison to day 0 of transplantation (Fig. 1). Two patients died due to transplantation-related toxicity. Two other patients rejected the transplanted marrow and later received their autologous backup marrow. By contrast, in those patients who received the autologous BMT as rescue, the LDH levels increased to pre-transplant levels (data not shown).

DISCUSSION

The profound and life-threatening anemia in patients with β-thalassemia is ascribed primarily to ineffective erythropoiesis, characterized by intramedullary hemolysis, elevated LDH levels, low levels of haptoglobin, hemopexin, and bizarre-looking red blood cells [4]. The pathophysiology relates directly to the accumulation of unmatched α chains bearing an obscure toxic effect. Yuan et al. [5] found evidence for accelerated programmed cell death (apoptosis) in erythroid precursors in the bone marrow of these patients. They demonstrated the typical ladder pattern of erythroblasts DNA breakdown products typical for apoptosis, explaining why most of these never survive to become mature erythrocytes.

The group of patients we described may indicate that a successful engraftment of marrow resulted in termination of the intramedullary hemolysis typical for β-thalassemia. In addition, rising levels of LDH post-transplant may serve as a marker for autologous recovery of host bone marrow. LDH may thus serve as an additional simple, reliable, rapid, and economic way to monitor disease status in β-thalassemia major patients post-BMT.

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